REMARKS

Claims 217-219, 225, 238, and 277 remain pending in this application. Claims 221, 283, and 285-287 have been cancelled without prejudice or disclaimer. Claims 1-216, 220, 222-224, 226-237, 239-276, 278-282, and 284 were previously canceled. Claims 217-219 and 277 have been amended. The amendments are made without prejudice to expedite the progress of the application.

Claim Amendments

Claim 217 has been amended to recite a method of inhibiting growth of a cancer cell comprising treating the cancer cell with a *linear* polypeptide. Support for the recitation of the polypeptide being linear is found throughout the specification, such as at Examples 3 and 10, and Fig. 16. Claim 217 also has been amended to incorporate the scope of claim 286. Further, in claim 217, SEQ ID No. 23 has been amended to correct a previously recited "D" amino acid residue to an "E" amino acid. This amendment corrects a typographical error. Support for this correction is found in the specification at page 92, line 9.

Claim 218 has been amended to use wording consistent with claim 217.

Claim 219 has been amended to depend from claim 217 and incorporates the subject matter of claim 285 (now cancelled) by specifying that the polypeptide comprises the amino acid sequence of either SEQ ID No. 2 or SEQ ID No. 3.

Claim 277 has been amended to state that the polypeptide of either claim 217 or claim 219 is up to 25 amino acids in length. Support for claim 277 is provided at page 49, lines 21 -23, of the specification as originally filed.

No new matter has been introduced by the claim amendments.

Rejections under 35 U.S.C §112, First Paragraph

Written Description

Claims 217, 219, 225, 238, 285, and 286 are rejected for alleged lack of written description. The Office Action alleges that Applicants were not in possession of a method of treating cancer comprising administration of SEQ ID Nos. 2, 3, 22, or 23 or a deletion mutant thereof without a

carrier peptide or auxiliary sequence to facilitate cellular entry. The rejection is respectfully traversed.

Since claim 218 was previously amended to recite a facilitator moiety, the Examiner is apparently asserting that claim 217 also should be restricted to a polypeptide as described above coupled to facilitator moiety for facilitating entry of the polypeptide into the cancer cell. Applicants submit that present claim 217 is directed to the *treatment* of a cell with the polypeptide *to inhibit the growth of the cell*. That is, the claimed invention relates to the *treatment of the cell* with the peptide to inhibit cancer cell growth, *not* any particular way the peptide is delivered into the cell or is otherwise provided.

In this regard, the disclosure of the invention throughout the specification teaches binding of polypeptides as described above to ERK2 in the absence of the polypeptide being coupled to a carrier peptide or other such facilitator moiety, see for instance, Example 3 at pages 84-87 and Example 10 at page 90.

Moreover, while the use of a penetratin derived peptide is exemplified in the specification to facilitate passage of the peptide into target cancer cells, various other such methods well known to a person of ordinary skill in the art are described in the specification. For example, the paragraph at page 54, lines 9-18, describes the use of liposome-mediated transfection as well as other methods. As such, it is submitted that present claim 217 is fully supported by the specification, and there is no reason to limit the invention as suggested by the Examiner when the skilled artisan would readily have appreciated that the specification describes methods for treating a cell without the need for any carrier peptide or auxiliary sequence.

The withdrawal of the rejection is respectfully requested.

Enablement

Claims 217-219, 221, 225, 238, 277, 283, and 285-287 are rejected as allegedly lacking enablement over the full scope of the claims. Specifically, the rejection alleges that the specification is not enabling for: (A) a polypeptide lacking a linker sequence or comprising a portion of a binding domain; (B) a polypeptide wherein the binding domain or a portion thereof is part of a cyclic peptide; and (C) a polypeptide lacking a facilitator domain. The rejection is respectfully traversed.

Regarding (A), claim 217 as amended provides for the binding domain provided by the polypeptide to be selected from the group consisting of RSKAKWQTGTNPLYR (SEQ ID No. 2), RARAKWDTANNPLYK (SEQ ID No. 22), and RARYEMASNPLYR (SEQ ID No. 23). Amended claim 217 further provides that the binding domain ***either includes the linker sequence***, which is non-essential for binding the MAP kinase, or ***excludes the linker***, in which case the opposite end portions of the recited sequences are joined and contiguous. Applicants believe that it would have been well within the capability of the ordinary skilled person to make and use such polypeptides based on the specification without using undue experimentation, as further discussed below.

The invention as claimed relates to the finding that ERK2 MAP kinase can bind to the β-integrin subunits β3, β5 and β6, and the localization and characterization of the amino acid sequences providing the respective binding domains, namely:

RSKAKWQTGTNPLYR (SEQ ID No. 2) (β6),

RARAKWDTANNPLYK (SEQ ID No. 22) (β3), and

RSRARYEMASNPLYR (SEQ ID No. 23) (β5).

The β3, β5, and β6 binding domains are characterized in that they each include an intervening amino acid linker sequence (underlined above) that is not essential for the binding of ERK2 MAP kinase.

That is, the linker sequence can be deleted to form a polypeptide comprising the *remaining* opposite amino acid sequence end regions of the binding domain joined directly to one another such that those amino acid sequences are contiguous, and to which ERK2 still binds. In this regard, the Examiner's attention is drawn to page 25, lines 3-9, of the specification which state that the binding domain can comprise regions linked together by intervening amino acids which do not directly participate in the binding interaction with the MAP kinase. In addition, the specification at page 26, lines 11-20, provides for ***deletions of amino acids*** from the binding domain while ***retaining binding activity***.

Thus, taking β6 for instance (as specifically exemplified in Example 3 of the specification), SEQ ID No. 2 includes the intervening amino acid linker sequence WQTGT which is interposed between the partial end sequences RSKAK (SEQ ID No. 4) and NPLYR (SEQ ID No. 5). The deletion of WQTGT provides the 10-mer peptide RSKAKNPLYR (SEQ ID No. 3) now specified in

claim 219. As stated at page 86, lines 14-19 of the specification, no reduction was observed in the binding of ERK2 to RSKAKNPLYR (SEQ ID No. 3) compared to RSKAKWQTGTNPLYR (SEQ ID No. 2). Moreover, simple sequence alignment of the amino acid sequences providing the β3 (SEQ ID No. 22) and β5 (SEQ ID No. 23) binding domains with that providing the β6 binding domain (SEQ ID No. 2), as is well within the expertise of a person of ordinary skill in the art, provides the corresponding intervening amino acid linker sequences WDTAN and YEMAS of β3 and β5.

The Examiner has expressed concern over the use of either of the partial sequences RSKAK (SEQ ID No. 4) and NPLYR (SEQ ID No. 5) alone as the binding domain. However, claim 217 as amended *excludes* the use of either of those peptides alone, as well as individual end amino acid sequences of the other respective binding domains, in the claimed method.

Present claim 217 requires the use of a linear polypeptide comprising either a binding domain defined by RSKAKWQTGTNPLYR (SEQ ID No. 2), RARAKWDTANNPLYK (SEQ ID No. 22) or RSRARYEMASNPLYR (SEQ ID No. 23), or a polypeptide comprising the binding domain in which the entire intervening amino acid linker sequence linking the opposite end regions of the binding domain together has been deleted. In the latter instance, the claim further requires that both of the opposite end amino acid regions of the binding domain remain present in the polypeptide *and that they are contiguous with one another.*

Applicants submit that the present claims leave no requirement for undue experimentation in order for the ordinary skilled person to determine which partial sequences of SEQ ID NO: 2, 22, or 23 provide functional binding to ERK2 MAP kinase. The withdrawal of the rejection is respectfully requested.

Regarding (B), the present claims have been amended to recite a <u>linear</u> polypeptide. Therefore, the Examiner's concern regarding cyclic peptides is now moot.

Regarding (C), as stated above in the response to the written description rejection, the claimed invention as described in the specification, for example at page 54, lines 9-18, does not rely exclusively on the use of a facilitator moiety for the treatment of cancer cells. Methods such as the use of liposome-mediated delivery, nanoparticulate carriers, and other methods of cellular delivery

that were well known to the skilled person, could have been used without the need for undue experimentation. Therefore, the withdrawal of the rejection is respectfully requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

MICHAEL VALENTINE AGREZ ET AL.

Date: March 9, 2010

By: /Holliday C. Heine/
Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

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